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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/802,220	03/17/2004	Masaki Sunami	227833	3562

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EXAMINER	
PAGONAKIS, ANNA	

ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
10/12/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Chgpatent@leydig.com

Office Action Summary	Application No.	Applicant(s)	
	10/802,220	SUNAMI ET AL.	
	Examiner	Art Unit	
	ANNA PAGONAKIS	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 15-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 15-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 sheet; 6/8/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed 4/5/2010 has been received and entered into the present application.

As reflected by the attached, completed copy form PTO/SB/08A (one page total), the Examiner has considered the cited references.

Applicant's arguments filed 4/5/2010 have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Applicant is reminded of the specie election made on 8/17/2007 of the disease hyperlipidemia and the compound S-[2-([[-(2-ethylbutyl)cyclohexyl]carbonyl]amino)phenyl] 2-methyl propanethioate.

Status of Claims

Claims 1-8 and 15-23 are currently under examination and the subject matter of the present Office Action.

Priority

This application claims benefit of 60/455,293 filed 3/17/2003; 60/460,521 filed 4/4/2003; 60/477,202 filed 6/10/2003 and 60/493,649 filed 8/8/2003.

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications, 60/455,293 filed 3/17/2003; 60/460,521 filed 4/4/2003; 60/477,202 filed 6/10/2003, fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. All claims are not adequately supported or enabled by the prior-filed applications the subject matter in claims 2-5 and 18-23. Specifically,

(i) 60/455,293 fails to disclose the limitations of claims: 2-7 and 16-23;

(ii) 60/460,521 fails to disclose the limitations of claims: 2-7 and 16-23;

(iii) 60/477,202 fails to disclose the limitations of claims: 2-7 and 16-23;

It is noted that Applicant is not entitled to the priority date in these application for all claims in the instant claim set because the information contained within the previous referred filings does not support the granting of an earlier filing date. Applicant is invited to guide the Examiner to where the appropriate disclosure of the limitations for the above mentioned claims are found the respective priority documents.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are rejected because they do not identify the structure, material, or acts set forth in the specification that would be capable of carrying out the functional properties recited in the claims, such as "wherein the maximum concentration of cholesteryl ester transfer protein inhibitor, or an active form thereof, in the bloodstream of a mammal is at least 0.35 ug/mL" (claim 18); " wherein the maximum concentration of cholesteryl ester transfer protein inhibitor, or an active form thereof, in the bloodstream of a mammal is at least 0.8 ug/mL (claim 19)"; "area under the plasma concentration time curve of the cholesteryl ester transfer protein inhibitor or active form thereof in the bloodstream of a mammal is at least 3.5 ug*h/mL" (claim 20); "area under the plasma concentration time curve of the cholesteryl ester transfer protein inhibitor or active form thereof in the bloodstream of a mammal is at least 7.5 ug*h/mL" (claim 21);

"wherein cholesteryl ester transfer protein activity in the bloodstream of a mammal is inhibited by at least 25 percent relative CETP activity pretreatment when the cholesteryl ester transfer protein inhibitor is administered at a daily dose of 600 mg of food" (claim 22); "wherein cholesteryl ester transfer protein activity in the bloodstream of a mammal is inhibited by at least 25 percent relative CETP activity pretreatment when the cholesteryl ester transfer protein inhibitor is administered at a daily dose of 600 mg of food" (claim 23).

Level of skill and knowledge in the art: The claimed function properties (i.e. AUC and blood plasma concentration) are achieved from specific formulations which contain specific ingredients. In the instant case, the active agent is a cholesteryl ester transfer protein inhibitor, specifically, JTT-705 administered at different dosages with or without the presence of food (pages 30-31 and 33-34).

Physical and/or chemical properties/Functional characteristics: Pages 30-31 and 33-34 detail the AUC values with respect to respective doses. The specification further states that the white tablets were prepared using standard tableting procedures and that each tablet, depending on the dosage of JTT-705, comprised additional components such as hydroxypropylmethyl cellulose, microcrystalline cellulose, lactose, talc, magnesium stearate, crospovidone and disintegrants administered with or without the presence of food (paragraphs [0018]-[0120]).

A review of the specification does not reveal disclosure on an example of a formulation that is used in the dosing regimen to obtain the instantly claimed pharmacokinetic parameters. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181,26 USPQ2d 1057 (Fed. Cir. 1993). Accordingly, the structure which makes up the formulation must be clearly and positively specified in order to place one of skill in the art in possession of the claimed tablets with the desired properties. It is precisely this structure that determines the desired properties and without which, one could not replicate the invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-8 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "substantially" in claim 5, is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not reasonably be appraised of the scope of the invention. The term is unclear because meets and bound of "substantially" is not clear. For instance, is the cholesteryl ester transfer protein inhibitor 99.9 percent crystalline or 51 percent crystalline. For purposes of prosecution, the term "substantially" is interpreted as greater or equal to 50 percent crystalline

Claim 16 recites obesity as a cardiovascular disorder. It is not clear from the art that obesity is in fact a cardiovascular disorder. However, it is not clear from the art that obesity is in fact a cardiovascular disorder. For example, an article posted on the American Heart Associations website authored by Kraus et al. (http://www.americanheart.org/presenter.jhtml?identifier=1818, Circulation 1998, 98) teaches that obesity is an important determinant of cardiovascular disease. However, the web site and article do not appear to suggest that obesity is in fact a cardiovascular disease. Thus, where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "obesisty" in claim 16 is used by the claim to mean "a cardiovascular disease", while the accepted meaning is "a condition that is an important determinant of cardiovascular disease." The term is indefinite because the specification does not clearly redefine the term.

Claim 19 recites "or active form thereof" of a cholesteryl ester protein inhibitor. The disclosure does not seem to teach an "active form thereof" of a cholesteryl ester protein inhibitor. It is not clear from the

disclosure what Applicant considers an "active form thereof" to be. For instance, "active form thereof" can be interpreted to include metabolites of a cholesteryl ester protein inhibitor.

Response to Applicant's Remarks

Applicant alleges that it is clear that the specification describes how to ascertain the requisite degree of "substantially crystalline." Specifically, Applicant guides the Examiner to paragraph [0078]. This is not persuasive. It is not clear how the measurement of the possible crystalline content which x-ray diffraction, SEM analysis and DSC, provides a "requisite" degree of guidance with regard to the term "substantially". It appears that Applicant is implying that crystallization measurement techniques of paragraph [0078] can allow one to determine the amount of crystalline present. However, it remains that Applicant has not guided the Examiner as to where a definition of "substantially" is found in the specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 7-8 and are rejected under 35 U.S.C. 103(a) as being unpatentable over Ault et al. (U.S. 2002/0123459) in view of Gumkowski et al. (U.S. 2003/0022944 A1)

Ault et al. teaches a composition suitable for oral delivery of pharmaceutically active agents, comprising a therapeutically effective amount of a pharmacologically active agent; a crospovidone or povidone; and a delivery agent for said pharmacologically active agents (abstract). Furthermore, the reference teaches the composition containing crospovidone versus the comparative compositions which do not contain crospovidone, resulting the greatly enhanced oral bioavailability of the formulations (paragraph [0084]).

Ault et al. is silent on the increasing the bioavailability of JTT-705.

Gumkowski et al. teach that CETP inhibitors, such as the elected compound, S-[2-([[-(2-ethylbutyl)cyclohexyl]carbonyl]amino)phenyl] 2-methyl propanethioate, alternatively known as JTT-705, are generally hydrophobic and thus have extremely low solubility and thus have low oral bioavailability (paragraph [0002] and [1159]). Various attempts have been made to improve the aqueous concentration of CETP inhibitors, but generally have met with limited success (paragraph [0010]). The preferred dose is at least 30 mg and further it is taught that CETP inhibitors can be administered with food (paragraph [0012 and [0120]).

One of ordinary skill in the art would have been motivated to substitute the pharmacologically active agent in Ault et al. with that of JTT-705. One would have been motivated to do so and have a reasonable expectation of success because JTT-750 is known to have a low oral bioavailability while crospovidone is known to achieve a great enhancement in oral bioavailability.

With respect to claim 7, the ratio of the CETP inhibitor, JTT-705, and crospovidone is within the skill of the artisan at the time of the invention and would not have required undue experimentation or have been outside the realm of knowledge generally available to the skilled artisan. Factors that would have been taken into consideration when making such a determination would have included, but not have been limited to, the age, weight, sex, diet and medical condition of the patient, severity of the disease, route of administration, pharmacological considerations, e.g., activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, the ratio that would have

actually been employed would have been expected to vary widely and, in the absence of evidence to the contrary, would not have been inconsistent with that which is presently claimed.

Claims 2-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ault et al. (U.S. 2002/0123459) in view of Gumkowski et al. (U.S. 2003/0022944 A1) as applied to claims 1 and 7-8 above and further in view of Cayman Chemical Company (Cayman Currents, Summer 2002).

The combination of Ault et al. (U.S. 2002/0123459) in view of Gumkowski et al. (U.S. 2003/0022944 A1) is set forth supra. The combination is silent on the JTT-705 in crystalline form.

Cayman Chemical teaches that JTT-705 is an inhibitor of cholesteryl ester transfer protein (CETP) which is manufactured as a solid crystalline. Further, JTT-705 has been found to attenuate induced atherosclerosis (page 9).

One of ordinary skill in the art would have been motivated to administer JTT-705 as a crystalline solid because it is known to be manufactured in this form. Further, one would have motivated to do so in order to treat atherosclerosis which it is known to do in this form, per Cayman Chemical.

Claims 15-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ault et al. (U.S. 2002/0123459) in view of Gumkowski et al. (U.S. 2003/0022944 A1) in view of Somers (U.S. 6,147,250).

Ault et al. teaches a composition suitable for oral delivery of pharmaceutically active agents, comprising a therapeutically effective amount of a pharmacologically active agent; a crospovidone or povidone; and a delivery agent for said pharmacologically active agents (abstract). Furthermore, the reference teaches the composition containing crospovidone versus the comparative compositions which do not contain crospovidone, resulting the greatly enhanced oral bioavailability of the formulations (paragraph [0084]).

Ault et al. is silent on the increasing the bioavailability of JTT-705.

Gumkowski et al. teach that CETP inhibitors, such as the elected compound, S-[2-([[-(2-ethylbutyl)cyclohexyl]carbonyl]amino)phenyl] 2-methyl propanethioate, alternatively known as JTT-705, are generally hydrophobic and thus have extremely low solubility and thus have low oral bioavailability (paragraph [0002] and [1159]). Various attempts have been made to improve the aqueous concentration of CETP inhibitors, but generally have met with limited success (paragraph [0010]). The preferred dose is at least 30 mg and further it is taught that CETP inhibitors can be administered with food (paragraph [0012 and [0120]).

Somers teaches that hyperlipidemia is the elevation of LDL cholesterol. Therefore, drugs commonly used to lower LDL levels are administered (column 5, lines 8-10).

One of ordinary skill in the art would have been motivated to administer a CETP inhibitor, such as JTT-705, for the treatment of hyperlipidemia because CETP inhibitors, such as JTT-705, are known to decrease LDL cholesterol which is necessary in order to treat hyperlipidemia. Further, one would have been motivated to administer crospovidone in combination with JTT-705 in order to ensure oral bioavailability of the pharmacological agent. one of ordinary skill in the art would have a reasonable expectation of success because crospovidone is well known in the art to enhance oral bioavailability of pharmacological agents.

With respect to claims 18-23, the AUC and the amount of cholesteryl ester transfer protein activity in the bloodstream is necessarily present with the administration of JTT-705. Further, it is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

With respect to the dosages of claims 22-23, the variation of dosage of the elected CETP with food, is within the skill of the artisan at the time of the invention and would not have required undue experimentation or have been outside the realm of knowledge generally available to the skilled artisan.

Factors that would have been taken into consideration when making such a determination would have included, but not have been limited to, the age, weight, sex, diet and medical condition of the patient, severity of the disease, route of administration, pharmacological considerations, e.g., activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, the ratio that would have actually been employed would have been expected to vary widely and, in the absence of evidence to the contrary, would not have been inconsistent with that which is presently claimed.

Response to Applicant's Remarks

Applicant alleges that JTT-705 is "one of the hundreds of disparate CETP inhibitors" disclosed in Gumkowski et al. and further there is no guidance contained as to why one would choose JTT-705. Applicant appears to be of the persuasion that, because Gumkowski et al disclose CETP inhibitors in addition to the one instantly elected, this somehow constitutes a complete lack of teaching of the claimed compound and/or constitutes a teaching away from the instantly claimed compound. This is not persuasive. A preferred or exemplified embodiment does not constitute a teaching away from other embodiments disclosed within the four corners of the reference, including non-preferred embodiments. Applicant is reminded that the disclosure of a reference must be considered as expansively as is reasonably possible to determine the full scope of the disclosure and, as a result, is most certainly most limited to that which is preferred and/or exemplified. Thus, the fact that other compounds may be exemplified, claimed and/or preferred does not negate or direct the artisan away from the broader teaching of the reference, which expressly provides for, and, thus, clearly contemplates the use the elected CETP inhibitor. A reference will constitute a teaching so long as the disclosure clearly describes and enables such an embodiment, which, in the present case, such description is clearly found in Gumkowski et al. The fact that the reference may teach embodiments that differ from Applicant's own invention does not negate, or teach away from, the teachings of the reference as a whole and what the reference as a whole would have reasonably suggested to one having ordinary skill in the art at the time of the invention.

Applicant alleges that Ault et al. is drawn to calcitonin which is not a CETP inhibitor and is structurally diverse from JTT-705. This is not found persuasive. Though calcitonin is not a CETP inhibitor, Ault et al. clearly teaches that the claimed crospovidone is known to enhance oral bioavailability of agents and further CETP inhibitors, including the instantly elected CETP inhibitor, is known to have low oral bioavailability. Applicant is again reminded that rejections made under 35 U.S.C. 103(a) are based upon the combination of references. As a result, focusing solely on the discrete teachings of each of the cited references is tantamount to examining each of them inside of a vacuum and fails to be persuasive in establishing non-obviousness because it is the *combined* teachings that are the basis for a proper conclusion of obviousness, not each individual reference alone. In other words, it must be remembered that the references are relied upon in combination and are not meant to be considered separately. To properly conclude obviousness of an invention *does not require the claimed invention to be expressly suggested in its entirety by any one single reference under 35 U.S.C. 103(a).* Rather, the test is *what the combined teachings* of the references would have suggested to those of ordinary skill in the art. Please reference *In re Young*, 403 F.2d 754, 159 USPQ 725 (CCPA 1968) and *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 15-23 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 10-11, 16-21, 34-40 and 53-58 of U.S. Patent 7,276,536 (Urata et al.) in view of Ault et al. (U.S. 2002/0123459) and Gumkowski et al. (U.S. 2003/0022944 A1) and Cayman Chemical Company (Cayman Currents, Summer 2002) and Somers (U.S. 6,147,250).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claims because the examined claims are either anticipated by, or would be obvious over the reference claims.

The claims of '536 are drawn increasing the bioavailability, increasing the absorption, treatment of a cardiovascular disorder and decreasing LDL with administration of the elected S-[2-([[-(2-ethylbutyl)cyclohexyl]carbonyl]amino)phenyl] 2-methyl propanethioate.

The claims of '536 fail to teach (i) administration with crospovidone; (ii) the crystalline form of to S-[2-([[-(2-ethylbutyl)cyclohexyl]carbonyl]amino)phenyl] 2-methyl propanethioate as well as the AUC and activity of CETP in the bloodstream.

Ault et al. teaches a composition suitable for oral delivery of pharmaceutically active agents, comprising a therapeutically effective amount of a pharmacologically active agent; a crospovidone or povidone; and a delivery agent for said pharmacologically active agents (abstract). Furthermore, the reference teaches the composition containing crospovidone versus the comparative compositions which do not contain crospovidone, which results in enhanced oral bioavailability (paragraph [0084]).

Ault et al. is silent on the administration of the crystalline form of the elected compound and the treatment of hyperlipidemia.

Gumkowski et al. teach that CETP inhibitors, such as the elected compound, S-[2-([[-(2-ethylbutyl)cyclohexyl]carbonyl]amino)phenyl] 2-methyl propanethioate, alternatively known as JTT-705, are generally hydrophobic and thus have extremely low solubility and thus have low oral bioavailability (paragraph [0002] and [1159]). Various attempts have been made to improve the aqueous concentration of CETP inhibitors, but generally have met with limited success (paragraph [0010]). The preferred dose is at

least 30 mg and further it is taught that CETP inhibitors can be administered with food (paragraph [0012 and [0120]).

Somers teaches that hyperlipidemia is the elevation of LDL cholesterol. Therefore, drugs commonly used to lower LDL levels are administered (column 5, lines 8-10).

Cayman Chemical teaches that JTT-705 is an inhibitor of cholesteryl ester transfer protein (CETP). Further, JTT-705 has been found to attenuate induced atherosclerosis (page 9).

One of ordinary skill in the art would have been motivated to administer a CETP inhibitor, such as JTT-705, for the treatment of hyperlipidemia because CETP inhibitors, such as JTT-705, are known to decrease LDL cholesterol which is necessary in order to treat hyperlipidemia. Further, one would have been motivated to administer crospovidone in combination with JTT-705 in order to ensure oral bioavailability of the pharmacological agent. one of ordinary skill in the art would have a reasonable expectation of success because crospovidone is well known in the art to enhance oral bioavailability of pharmacological agents. Further, One of ordinary skill in the art would have been motivated to administer JTT-705 as a crystalline solid because it is known to be manufactured in this form. Additionally, one would have motivated to do so in order to treat atherosclerosis which it is known to do in this form, per Cayman Chemical.

Conclusion

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 7am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AP

/Brandon J Fetterolf/
Supervisory Patent Examiner, Art Unit 1628